

Pancytopenia in a Young Male Patient with Inflammatory Bowel Disease

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Case Description

A 20-year-old male college student with a history of Crohn's disease was noted to have pancytopenia on routine lab monitoring. He was diagnosed with stricturing Crohn's disease of the terminal ileum and colon over 10 years ago when he presented with weight loss and bloody diarrhea. He struggled with perianal fistulizing disease periodically. His Montreal classification was A1 L3 B2p. Previous therapies included corticosteroids, mesalamine, azathioprine, 6-MP, infliximab, adalimumab, methotrexate, and certolizumab often in combination. At presentation he was on vedolizumab 300 mg intravenous infusion every 8 weeks. He had last been on tumor necrosis factor-alpha (TNF- α) therapy 4 years and thiopurines 1 year before presentation. His only other medication was cimetidine for acne vulgaris. His most recent colonoscopy showed diffuse ulceration scattered throughout the colon, but worst in the sigmoid colon and rectum (Figure A). Biopsies showed chronic active colitis with non-caseating granulomas.

In clinic, he reported 1-2 bowel movements per day with blood once a week. He had no abdominal pain, no weight loss, no fevers, and no nausea or vomiting. No sick contacts were noted. He had never smoked and did not drink alcohol. His family history was notable for a mother with basal cell carcinoma of the skin and no family members with inflammatory bowel disease (IBD) or colon cancer.

Physical examination revealed a temperature of 36.7° Celsius, heart rate 86 beats per minute, and blood pressure 119/74 mmHg. The young man was in no acute distress with a BMI of 19.1 kg/m². He had conjunctival pallor. Oropharynx was without aphthous ulcers. Exam of abdomen was soft and mildly tender on the left side with palpable splenomegaly. Joint and skin exams were normal. There was no palpable lymphadenopathy. Laboratory evaluation revealed a white cell count of $1.5 \times 10^9/L$, hemoglobin of 11.9 g/dL, and platelet count of $111 \times 10^9/L$. Differential revealed neutropenia (ANC 300) and lymphopenia (ALC 700). Fecal calprotectin was 440 mcg/g. Computed tomography showed massive splenomegaly (Figure B).

Multiple Choice Question

Q: Which of the following is the most appropriate next step in this patient's workup:

- A: Test for viral disease
- B: Check for nutritional deficiency
- C: Stop cimetidine
- D: Obtain a bone marrow biopsy

Discussion

This patient's presentation is concerning for hepatosplenic T-cell lymphoma (HSTCL), the diagnosis is confirmed by bone marrow biopsy [answer D].

Pancytopenia is a worrisome finding in IBD patients. It can be seen with viral infections such as HIV, CMV, and EBV [answer A], but, our patient's lack of sick contacts, new sexual partners, or symptoms make viral illness less likely. Patients with Crohn's are at risk for nutritional deficiencies of iron, copper, vitamin B12, and folate that may cause cytopenias, but his ominous splenomegaly makes a nutritional etiology less probable [answer B]. Myelotoxicity is a known adverse effect of cimetidine, an H2 blocker; however, his age and gender are key clues to consider a lymphoproliferative disorder before a medication side effect [answer C].

HSTCL is a rare, highly fatal condition associated with the use of TNF- α drugs and immunomodulators.^{1,2,3} It typically presents with weight loss, fevers, night sweats, abdominal pain, marked hepatosplenomegaly, and pancytopenia.¹ The general population risk of HSTCL is 1:5,158,750 and 1:45,000 in those immunosuppressed.³ This risk increases to 1:21,947 for all patients on thiopurines combined with TNF- α medications.³ The absolute risk for males <35 years old on thiopurines is 1:7,404 and for males <35 years old on thiopurines combined with TNF- α drugs is 1:3,534.³ As such, thiopurines are often avoided or used cautiously in young, male IBD patients – risk duration is unknown. A link with anti-integrin drugs is not established. HSTCL is confirmed with bone marrow biopsy; this patient's had increased blasts, hypercellular marrow, and clonal proliferation (Figure C). Flow cytometry and staining revealed an infiltrate of atypical T-cells. Cytogenetic analysis showed isochromosome 7q. Diffusely hypermetabolic bone marrow, enlarged spleen, and enhancing sigmoid colon consistent with his IBD history (Figure D) were seen on PET scan. Treatment of HTSCL is chemotherapy and hematopoietic stem cell transplant.¹ This patient achieved remission with chemotherapy then salvage treatment and multiple stem cell transplants. He is well a few years after diagnosis exceeding the median <12-month survival predicted by the literature.¹ This clinical vignette highlights the importance of recognizing this rare, but potentially fatal complication of IBD therapy: HSTCL.

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